Remarks

Reconsideration of this Application is respectfully requested.

Claims 36, 37, 40, 41, 43, 44, 46-49, 58 and 59 are pending in the application, with claim 36 being the sole independent claim.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 36, 37, 40, 41, 43, 44, 46-49 and 58 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. *See* October 5, 2005 Office Action, page 2. Applicants respectfully traverse this rejection for the reasons set forth in the Reply filed on July 14, 2005. Applicants submit the following additional remarks.

The written description rejection is based on the Examiner's position that the claims "are directed toward a genus of methods for identifying separin inhibitors using *any substrate*." *See* July 23, 2004 Office Action, page 2 (emphasis added). The Examiner appears to believe that the written description requirement necessarily requires that, for every element generically recited in a claim, the specification must disclose a structure

common to every possible species of the recited generic element. *See* October 5, 2005 Office Action, page 3. In the Examiner's words:

> [T]he specification does not describe a substantial portion of an amino acid sequence that is common to all members of the genus of separin substrates. Thus, the skilled artisan cannot predict the structure of other species encompassed by the genus separin substrates, fragments, and variants thereof."

See Id.

The Examiner's application of the written description requirement in this context is legally incorrect. First, Applicants emphasize that the claims are not directed to separin substrates. The claims are directed to *methods* that include the use of separin substrates. This is a critical distinction that must be taken into account when assessing compliance with the written description requirement. *See* discussion presented below.

When generic elements of a claim (*e.g.*, separin substrates comprising the amino acid sequence EXXR) are so well known and thoroughly characterized in the art that their recitation alone is sufficient to convey distinguishing information regarding their identity, the written description requirement for those elements is fully satisfied. *See, Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 U.S.P.Q.2d 1385, 1398 (Fed. Cir. 2003). Since the written description issue in *Amgen* is very similar to the written description issue raised in the present Office Action, a brief discussion of the *Amgen* case is presented below and a copy of the case is provided herewith as Exhibit 1.

In *Amgen*, the claims at issue were directed to methods for producing a glycosylated erythropoietin polypeptide. *See Amgen* at 1390. The claimed methods included, *inter alia*, the step of "growing, under suitable nutrient conditions, *vertebrate cells* comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6." *See id.* Also at issue were dependent claims that specified that the cells were *mammalian cells*. *See Amgen* at 1391. Just as separin substrates comprising an amino acid sequence EXXR in the present claims are not being claimed *per se*, the claims at issue in *Amgen* were not directed to vertebrate cells or mammalian cells *per se*. Rather, the cells were simply an element used in the practice of the claimed methods.

The defendants in *Amgen* asserted that the claims lacked adequate written description because "Amgen failed to sufficiently describe the use of all vertebrate and mammalian cells." *See Amgen* at 1397. Like the Examiner in the present case, the defendants in *Amgen* cited *University of California v. Eli Lilly and Co.* 43 USPQ 2d 1398 (Fed. Cir. 1997) to support the assertion of inadequate written description. *See Amgen* at 1398. The Federal Circuit made it clear, however, that *Eli Lilly* does not apply when, as here, the subject matter in question is well known and fully appreciated by persons of ordinary skill in the art. According to the court:

> the claim terms at issue here are not new or unknown biological materials that ordinary skilled artisans would easily miscomprehend. Instead, the claims of Amgen's patents refer to types of cells that can be used to produce recombinant human EPO...*the words "vertebrate" and "mammalian" readily "convey[]*

> *distinguishing information concerning [their] identity" such that one of ordinary skill in the art could "visualize or recognize the identity of the members of the genus.*" Indeed, the district court's reasoned conclusion that the specification's description of producing the claimed EPO in two species of vertebrate or mammalian cells adequately supports claims covering EPO made using the genus of vertebrate or mammalian cells, renders *Eli Lilly* listless in this case.

Id. at 1398 (internal citations omitted, emphasis added).

Thus, even though Amgen's patents described only "two species of vertebrate or mammalian cells," the Federal Circuit found such disclosure to provide adequate written description support for the entire genus of vertebrate or mammalian cells used to produce EPO according to the claimed methods. The court's decision was based on two principle factors:

1. That the claim terms at issue ("vertebrate" and "mammalian") did *not* refer to new or unknown biological materials that ordinary skilled artisans would easily miscomprehend; and
2. That the words "vertebrate" and "mammalian," as used in the claims, readily conveyed distinguishing information concerning their identity such that one of ordinary skill in the art could visualize or recognize the identity of members of the genus.

When the reasoning of *Amgen* is applied in the context of the present claims, it is clear that the written description requirement is more than adequately satisfied for separin substrates comprising an amino acid sequence EXXR.

First, the term "separin substrate" like the terms "vertebrate" and "mammalian," does not refer to new or unknown biological materials that ordinary skilled artisans would easily miscomprehend. Separin substrates in general, and those comprising the amino acid sequence EXXR in particular, were well known and characterized prior to the effective filing date of the present application. *See, e.g.*, Applicants' Reply filed July 14, 2005, pages 4-6. Accordingly, at the time of the effective filing date of the present application, separin substrates (including separin substrates comprising the amino acid sequence EXXR) certainly were not new or unknown biological materials.

Second, the expression "separin substrate . . . comprising the amino acid sequence EXXR" readily conveys distinguishing information concerning the identity of the substrates so that persons of ordinary skill in the art could recognize the identities of members of the genus. Persons of ordinary skill in the art would readily understand from the claim terms alone that the substrates used in the practice of the claimed methods (a) include the EXXR amino acid motif, and (b) are capable of being cleaved by separin. Thus, a skilled person would be able to readily distinguish the separin substrates used in the practice of the claimed methods from peptides that fall outside the scope of the claim language (*i.e.*, peptides that lack the EXXR amino acid motif and/or are not capable of being cleaved by separin).

In *Amgen*, the specification at issue disclosed two species of vertebrate or mammalian cells and was held to provide adequate written description support for these

genuses. Here, the specification discloses several exemplary EXXR-containing separin substrates, including the following working examples:

(i) yeast Scc1 tagged with HA epitopes (Examples 2 and 3 (pages 34-35));

(ii) purified yeast Scc1 (Example 5 (pages 36-37));

(iii) untagged human SCC1 (Example 9 (page 38)); and

(iv) human SCC1 tagged with Myc epitopes (Examples 10-13, pages 38-40)).

See specification at page 7, lines 9-13, and at page 21, lines 8-10. There is no indication that the inventors intended to limit in any way the kinds of separin substrates that can be used in the claimed methods. Just as a person of ordinary skill in the art would have appreciated that the invention at issue in *Amgen* included the use of *any* vertebrate or mammalian cell to produce EPO, a person of ordinary skill in the art would have appreciated that the present invention includes the use of *any* separin substrate comprising the amino acid sequence EXXR that is capable of being cleaved by separin.

The Examiner's attention is also directed to Example 18 of the USPTO's "Synopsis of Application of Written Description Guidelines" (available at http://www.uspto.gov/web/menu/written.pdf, copy submitted herewith as Exhibit 2). This Example illustrates an analysis of the written description provided for a process claim where the novelty is in the method steps. The claim at issue in this Example is as follows:

A method of producing a protein of interest comprising;

obtaining *Neurospora crassa* mitochondria,

> transforming said mitochondria with a expression vector comprising a nucleic acid that encodes said protein of interest,
>
> expressing said protein in said mitochondria, and
>
> recovering said protein of interest.

The specification shows actual reduction to practice of a single embodiment: the expression of β-galactosidase. The claimed process, however, involves the use of *any* nucleic acid that encodes *any* protein of interest, a virtually unlimited genus. Nonetheless, the Example concludes that the claimed invention is adequately described. According to the analysis provided in this Example:

> The art indicates that there is no substantial variation within the genus because there are a limited number of ways to practice the process steps of the claimed invention.
>
> The single embodiment is representative of the genus based on the disclosure of *Neurospora crassa* mitochondria as a gene expression system, considered along with the level of skill and knowledge in the gene expression art. One of skill in the art would recognize that applicant was in possession of all of the various expression methods necessary to practice the claimed invention.

Significantly, in assessing the written description of this hypothetical claim, the USPTO's Example does not even question whether the specification provides adequate

description of the entire genus of nucleic acid encoding a protein of interest because the nucleic acid is *not itself being claimed.* Thus, the analysis properly focuses on whether the *process* is adequately described, not whether the individual elements used in the practice of the process (*e.g.*, the different types of nucleic acids) are adequately described.

Analogously, separin substrates comprising the amino acid sequence EXXR in the present claims are not themselves being claimed; they are simply elements used in the practice of the claimed methods. Thus, the written description analysis should focus on whether or not the *methods* are adequately described, not whether separin substrates comprising the amino acid sequence EXXR are adequately described (although they certainly are adequately described, as noted above and in Applicants' previous responses).

Moreover, Example 18 of the USPTO's Guidelines emphasizes the need to consider the level of skill and knowledge in the relevant art in assessing adequacy of written description. As discussed previously, the level of skill and knowledge in the art concerning separin substrates was high, especially considering that multiple substrates had been identified and characterized at the time of the effective filing date of the present application. *See* Applicants' Reply filed on July 14, 2005, pages 6-7. (The Examiner has not presented any evidence to suggest that the level of skill and knowledge in the art of separin substrates was not high.) The high level of skill and knowledge in the art reinforces the conclusion that the written description requirement is fully satisfied for the currently presented claims.

The Examiner's application of the written description requirement in the present case appears to assume that separin substrates comprising the amino acid sequence EXXR are new compounds that are being directly claimed; however, as mentioned above, this is not the

case. Numerous species of separin substrates comprising the amino acid sequence EXXR had been identified and studied prior to the effective filing date of the present application. Persons of ordinary skill in the art would clearly appreciate and visualize the full range of separin substrates included in the practice of the present claims without any need for disclosure of common structural characteristics beyond the recitation of the EXXR sequence. The present claims are directed to *methods* that involve the use of such substrates. The Examiner's basis for rejecting the claims due to an alleged lack of description of "a substantial portion of an amino acid sequence that is common to all members of the genus of separin substrates" is therefore legally improper.

Finally, Applicants maintain that the Examiner's rationale for the written description rejection (which, as noted above, is itself clearly legally flawed) cannot in any event apply to claim 58. Claim 58 specifies that the separin substrate is human SCC1. According to the Examiner, "the recitation of the name 'human SCC1' does not define any structural features and amino acid sequences commonly possessed by the genus." *See* October 5, 2005 Office Action, page 4. The term "human SCC1," however, is explicitly defined in the specification as having SEQ ID NO:1. *See* specification, page 19, lines 30-31. Human SCC1 is a well defined molecule with a known and disclosed amino acid sequence. Persons of ordinary skill in the art would immediately know which protein is being referred to by the term "human SCC1." The Examiner has not presented any evidence to suggest that a person of ordinary skill in the art would consider the term "human SCC1" to represent a genus of proteins, or that a skilled person would not be able to "visualize or recognize the identity" of human SCC1 by its name alone. More importantly, the Examiner has presented no legal

authority to support the astounding position that a patent application which provides the amino acid sequence of a defined polypeptide does not adequately describe that polypeptide.

In view of the current state of the law on adequacy of written description (*e.g.*, *Amgen*) and the USPTO's own guidelines on this topic, it must be concluded that the written description requirement of § 112, first paragraph, is fully satisfied for the currently presented claims. Applicants respectfully request that this rejection be reconsidered and withdrawn.

II. Claim Rejections Under 35 U.S.C. § 103

Claims 36, 37, 40, 41, 43, 44 and 48 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Brown *et al.*, *Analyt. Biochem. 217*:139-147 (1994) ("Brown") in view of Ciosk *et al.*, *Cell 93*:1067-1076 (1998) ("Ciosk"). *See* October 5, 2005 Office Action, page 4. Applicants respectfully traverse this rejection for the reasons set forth in the Reply filed on July 14, 2005. Applicants submit the following additional remarks.

As noted in Applicants' previous response, the Examiner in making this rejection has relied on Ciosk for allegedly "teach[ing] a recombinant separin called Esp1p and its yeast substrate Scc1." *See* March 14, 2005 Office Action, page 4. The Examiner's reliance on Ciosk is flawed for two reasons: (1) there is nothing in Ciosk to indicate that Scc1p is a proteolytic substrate of Esp1p; and (2) there is no suggestion whatsoever in Ciosk that Esp1 is a protease at all. In fact, Ciosk explicitly suggests that Esp1p may function by mechanisms such as altering the nuclear concentration of Ca^{2+} -- a mechanism which does not in any way suggest a proteolytic role for Esp1p. *See* Applicants' Reply filed on July 14, 2005, pages 13-14.

The Examiner has neglected to address the above points as set out in Applicants' previous response. Rather, the Examiner, at pages 4-5 of the Office Action, has relied on passages from *Applicants' own specification* to support a legally improper theory of inherency. According to the Examiner:

> Thus, the examiner takes the position that the Esp1p taught by Ciosk et al. *inherently* is a separin and the yeast substrate Scc1 disclosed by Ciosk et al. *inherently* is a substrate for the taught Esp1p.

See October 5, 2005 Office Action, page 5 (emphasis added). This reasoning is directly contrary to legal precedent and cannot stand as a basis for an obviousness rejection.

First, it is well established that, in an obviousness rejection, the teaching or suggestion to make a claimed combination must be found in the prior art, not in Applicants' disclosure. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Clearly, the Examiner cannot rely on passages from Applicants' own specification to support a theory of motivation to combine references.

Second, it is equally well established that an obviousness rejection cannot be based on what is asserted to be *inherent* in a reference. *See In re Spormann*, 150 USPQ 449, 452 (CCPA 1966). That which is inherent cannot be obvious, since inherent information "is not necessarily known . . . [and] Obviousness cannot be predicated on what is unknown." *Id.* *See also In re Newell*, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989) ("a retrospective view of inherency is not a substitute for some teaching or suggestion which

supports the selection and use of the various elements in the particular claimed combination.") Since the courts have explicitly rejected the possibility of using inherency to support an obviousness rejection, the Examiner's assertion of obviousness cannot be maintained.

The Examiner has presented no evidence outside of Applicants' own disclosure to indicate that Ciosk would have in any way suggested to a person of ordinary skill in the art that Scc1p is a proteolytic substrate of Esp1p or that Esp1p is a protease. Without some indication *in the prior art* that Esp1p is a protease and that Scc1p is a proteolytic substrate of Esp1p, a person of ordinary skill in the art would have had no motivation to combine Ciosk with Brown. Without a motivation to combine references, the obviousness rejection cannot be maintained. Applicants respectfully request that this rejection be reconsidered and withdrawn.

III. Claim Objection

Claim 59 was objected to as being dependent upon a rejected base claim. *See* October 5, 2005 Office Action, page 5. Claim 59 depends from claim 46, which in turn depends from claim 36. As discussed above, the rejections of claims 36 and 46 are in error and should be withdrawn. Accordingly, Applicants respectfully submit that the objection to claim 59 is also in error and should be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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